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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/881,446	06/13/2001	Robert A. Star	4239-58570	6918

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EXAMINER

COUNTS, GARY W

ART UNIT PAPER NUMBER

1641

DATE MAILED: 04/16/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/881,446

Applicant(s)

STAR ET AL.

Examiner

Gary W. Counts

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 03 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-12, 14-19, 21, 22 and 24-37 is/are pending in the application.
- 4a) Of the above claim(s) 17-19, 21, 22 and 24-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12, 14-16 and 35-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3. 6) ☐ Other:

## **DETAILED ACTION**

### **Status of the claims**

The amendment and election filed on February 3, 2003 is acknowledged and has been entered.

### ***Election/Restrictions***

1. Applicant's election with traverse of Group 1, claims 1-16 and 35-37 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that Groups I-III are drawn to or based on a linking claim 35. This is not found persuasive because Groups I-III are not drawn to a linking claim as defined in the MPEP 809.03. Please see groups A-D in MPEP 809.03. Claim 35 is a single subcombination to a plurality of individual patentably distinct combinations. And the previous office action correctly placed the subcombination with each combination. If the subcombination is patentable any combination within reason would be patentable where no statutory rejection exists. Applicant further argues that Groups I and II are different inventions of the same disclosed subject matter varying in breadth or scope of definition and that restriction is improper. This is not found persuasive because the previous office action clearly stated the different limitations that exist between the two groups, which require different search terms, and a different search strategy. Further, while searches would be expected to overlap, there is no reason to expect the searches to be coextensive. The requirement is still deemed proper and is therefore made FINAL.

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-12, 14-16 and 35-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 5 "components" is vague and indefinite. It is unclear what the term is referring to (i.e. cells, organelles, tissue fluid, etc.). There is no definition provided for the term in the specification.

Claim 4 "the presence of water" there is insufficient antecedent basis for this limitation. Further, it is unclear if the water is part of the aqueous solution or not. It is unclear what applicant is trying to encompass with the recitation "in the presence of water".

Claim 6 "a capture member" is vague and indefinite. There is no definition provided for the term in the specification. Is applicant applying an antibody or a substrate or a device such as a needle to the tissue sample or something else?

Claim 12 is vague and indefinite because it is unclear what structural and functional cooperative relationship exists between the primary and secondary antibodies and the tissue. Do the primary antibodies and the secondary antibodies bind to each other to form a complex, which in turn will bind a specific component of the tissue when later incubated with the tissue, or do the two antibodies bind to different components on the tissue? Further, it is unclear how one of the antibodies is fluorescent (i.e. does the antibody naturally fluoresce or is the antibody coupled to a fluorescent moiety?) See also deficiency in claim 9.

Claim 35 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. The preamble of the claim implies that a biological molecule is preserved however, it is not positively recited in the body of the claims. Further, it is unclear what structural and functional cooperative relationship exists between the elements recited in the claim such as the tissue, the target cells, the biological molecule and the fluorescent specific binding agent. Also, it is unclear how the tissue preserves a biological molecule.

Claim 35 the recitation "sufficient" is a relative term, which renders the claim indefinite. The term "sufficient" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See deficiencies throughout the claims. Further, on page 10, line 28 discloses a sufficient excess of fluorescent specific binding agent. The term sufficient or sufficient excess does not define the metes and bounds of the claim.

***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1 and 35 are rejected under 35 U.S.C. 102(a) as being anticipated by Fink et al (Immunostaining and Laser-Assisted Cell Picking for mRNA Analysis, Laboratory Investigation, March 2000 Vol 80, p. 327-333).

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Fink et al disclose a method for fluorescently labeling tissue. Fink et al disclose incubating the tissue with a FITC-conjugated antibody (fluorescent specific binding agent) for 3 to 10 minutes (p. 332). Fink et al also disclose the preservation of mRNA (biological molecule). Fink et al disclose identifying cells of the tissue and microdissecting the cells from the tissue.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1, 4-6, 9 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liotta et al (US 6,251,467) in view of Fink et al (Immunostaining and Laser-Assisted Cell Picking for mRNA Analysis, Laboratory Investigation, March 2000 Vol 80, p. 327-333).

Liotta et al disclose a method for microdissecting a tissue. Liotta et al disclose labeling molecules such as antibodies or fragments thereof (specific binding agent) which are directed to a specific cell or group of cells in the tissue sample. Liotta et al disclose that this coupling of the labeled antibody to the tissue provides for imaging the tissue with a camera (col 4, lines 15-67). Liotta et al disclose microdissecting the cells from the tissue sample by applying a transfer film (capture member) on the tissue sample and applying a laser energy to the cells (component of interest) to adhere the cells to the transfer film (col 11). Liotta et al also disclose that for mRNA analysis the

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tissue specimen can be placed on agarose and treated with agents to denature or otherwise inhibit Rnase (preserve mRNA) (col 8).

Liotta et al differ from the instant invention in failing to specifically teach that the label is fluorescent and that the fluorescent specific binding agent is directed in less than about five minutes.

Fink et al disclose a method for fluorescently labeling tissue. Fink et al disclose incubating the tissue with a FITC-conjugated antibody (fluorescent specific binding agent) for 3 to 10 minutes (p. 332). Fink et al also disclose the preservation of mRNA (biological molecule). Fink et al disclose identifying cells of the tissue and microdissecting the cells from the tissue. Fink et al disclose that the use of this immunofluorescence staining reduced the number of antibodies and incubation periods and thus provide more rapid protocols for immunofluorescence (abstract).

It would have been obvious to one of ordinary skill in the art to incorporate the use of a fluorescent label as taught by Fink et al into the method of Liotta et al because Fink et al shows that the use of this fluorescent label reduced the number of antibodies and incubation periods and thus provide more rapid protocols for immunofluorescence.

8. Claims 2, 3, 7, 8, 10, 11, 14-16, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liotta et al in view of Fink et al as applied to claims 1, 4-6 and 9 above, and further in view of Rushbrooke et al (US 4,922,092).

See above for teachings of Liotta et al and Fink et al.

Liotta et al and Fink et al differ from the instant invention in failing to provide an intensified image signal and a filter.

Rushbrooke et al disclose the use of an image intensifier coupled with a camera. Rushbrooke et al also disclose that the image intensifier can include a filter. Rushbrooke et al disclose that this image intensifier increased the photon coupling between the sources and the intensifier and enhances the number of photons available for supply to the detector (col 7).

It would have been obvious to one of ordinary skill in the art to incorporate an image intensifier as taught by Rushbrooke et al into the modified method of Liotta et al because Rushbrooke et al shows that that this image intensifier increased the photon coupling between the sources and the intensifier and enhances the number of photons available for supply to the detector.

With respect to the sufficient concentration of the specific binding agent and the exposure time of the specific binding reagent to the tissue as recited in the instant claims, the optimum concentration and the optimum exposure time can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill



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of the art.” Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

***Allowable Subject Matter***

9. Claim 12 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: the prior art of record neither teaches nor suggests pre-mixing a primary antibody and a secondary antibody, at least one of which is fluorescent, prior to exposing the tissue to the fluorescent specific binding agent to reduce a time of exposure of the tissue to the fluorescent specific binding agent.

The closest reference is Fink et al. (see above). Fink et al disclose exposing the tissue to a primary antibody and then subsequently exposing the tissue to a second fluorescent labeled antibody. Fink et al does not teach pre-mixing a primary antibody and a secondary antibody, at least one of which is fluorescent, prior to exposing the tissue to the fluorescent specific binding agent to reduce a time of exposure of the tissue to the fluorescent specific binding agent.

***Conclusion***

10. No claims are allowed.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

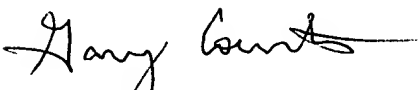
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Taylor et al (Immunohistochemistry: Principles and Practice, American Society for Microbiology, 1996, 369-379).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
Gary W. Counts  
Examiner  
Art Unit 1641  
April 14, 2003

  
CHRISTOPHER L. CHIN  
PRIMARY EXAMINER  
GROUP 1800/641  
4/14/03